Amendments to claims filed August 20, 2001
Atty Docket No. 5525-0044.10

1. (Amended) A nucleic acid reference library derived from pooled DNA from at least two sources, said library comprising a heterogeneous mixture of nucleic acid fragments, wherein

each said fragment[s comprise] (a) is a portion of a polymorphic subregion of a polymorphic consensus sequence derived from said pooled DNA or (b) is derived from a non-polymorphic subregion, [wherein]

each of said polymorphic subregions is bounded by first restriction sites and comprises an internal polymorphic restriction site which is different from said first site;

said polymorphic consensus sequence is the theoretical sequence obtained by (i) aligning said pooled DNA to provide maximum homology, and (ii) projecting each of said restriction sites onto said sequence; and

said library is enriched for fragments of type (a) relative to type (b) [other than those located between said polymorphic subregions].

2. (Amended) A nucleic acid reference library according to claim 1, wherein at least a subpopulation of said [library comprises] nucleic acid fragments further comprise[ing] oligonucleotide tags, [wherein] and different nucleic acid fragments are linked to different oligonucleotide tags.

3. (Amended) The nucleic acid reference library according to claim 2, [further comprising] wherein said fragments are contained within a replicable vector.

4. (Amended) The nucleic acid reference library according to claim 2, wherein said oligonucleotide tags comprise oligonucleotides of the form:

$$S_1S_2S_3 \ldots S_n$$

wherein each of $S_1$ through $S_n$ are subunits consisting of an oligonucleotide having a length from 3 to 9 nucleotides and are selected from a minimally cross-hybridizing set, n is in the range of from 4 to 10, and [wherein] said tag has a length in the range of from 12 to 60 nucleotides or base pairs.

5. (Amended) A composition comprising subpopulations of microparticles, wherein each subpopulation comprises at least one microparticle, said microparticle comprising a polymorphic probe, wherein the polymorphic probe[s] of each [the different] subpopulation[s are] is different from those of the other subpopulations, [said others] and comprises a portion of a polymorphic subregion of a polymorphic consensus sequence as recited in claim 1.

6. (Amended) The composition of claim 5, wherein each of said subpopulations further comprises a [unique] oligonucleotide tag[s], and different subpopulations comprise different tags.

7. (Amended) The composition according to claim 6, wherein each said oligonucleotide tag[s are] is positioned between said microparticle and said polymorphic probe.

8. (Amended) The composition according to claim 6, wherein each said oligonucleotide tags comprises an oligonucleotide[s] of the form:

$$S_1S_2S_3 \ldots S_n$$

wherein each of $S_1$ through $S_n$ are subunits consisting of an oligonucleotide having a length from 3 to 9 nucleotides and are selected from a minimally cross-hybridizing set, n is in the range of from 4 to 10, and [wherein] said tag has a length in the range of from 12 to 60 nucleotides or base pairs.

9. (Amended) An array comprising a solid support having defined regions on the surface thereof, wherein each region comprises a different polymorphic probe, and wherein each of said polymorphic probes comprises a portion of a polymorphic subregion of a polymorphic consensus sequence as recited in claim 1.

10. (Amended) The array of claim 9, wherein each of said regions further comprises an oligonucleotide tag, and different subpopulations comprise different tags.

11. (Amended) The array of claim [11] 10, wherein each said oligonucleotide tag[s are] is positioned between said surface and said polymorphic probe.

12. (Amended) The array according to claim 11, wherein each said oligonucleotide tag comprises an oligonucleotide[s] of the form:

$$S_1S_2S_3 \ldots S_n$$

wherein each of $S_1$ through $S_n$ are subunits consisting of an oligonucleotide having a length from 3 to 9 nucleotides and are selected from a minimally cross-hybridizing set, n is in the range of from 4 to 10, and [wherein] said tag has a length in the range of from 12 to 60 nucleotides or base pairs.

15. (Amended) A method of making a reference library comprising a mixture of heterogeneous nucleic acid fragments, comprising:

digesting pooled nucleic acid comprising first restriction sites with a first restriction endonuclease to produce a mixture of restriction fragments;

forming a first population of single stranded nucleic DNA fragments from a first subpopulation of said restriction fragments, wherein said first subpopulation [comprises a portion of said mixture] of restriction fragments [which] comprises a second restriction site which is different from said first restriction site; [and]

forming a second population of single stranded DNA fragments from a second subpopulation of said restriction fragments, wherein said second subpopulation [comprises a portion] of said restriction fragments [that] do not contain said second restriction site, and wherein said first single stranded DNA fragments [from said first subpopulation have] are complementary [sequences] to said second single stranded DNA fragments [from said second subpopulation] when[ever] said single stranded DNA fragments are derived from the same restriction fragment;

hybridizing the first and second populations of single stranded DNA fragments to form a population of duplexes; and

isolating said duplexes to form a reference population of restriction fragments.

16. (Amended) The method of Claim [16] 15, further comprising the step of pretreating said pooled nucleic acid to enrich for non-repetitive sequences.

18. (Amended) The method of claim [18] 17, wherein said first pool of test nucleic acids is from a population of individuals having a first phenotype and said second pool of test nucleic acids is from a population of individuals having a second phenotype.

19. (New) The method of claim 17, wherein said enriching comprises selecting fragments from said pools which lack said second restriction site, and said contacting comprises contacting said selected fragments with probes which contain said second restriction site.

20. (New) The method of claim 17, wherein said enriching comprises selecting fragments from said pools which contain said second restriction site, and said contacting comprises contacting said selected fragments with probes which lack said second restriction site.